REMARKS

Claims 1-3 and 31 are pending. Claims 3 and 31 have been canceled. Non-elected Claims 4-30 and 32-53 have been withdrawn. New Claims 54-57 have been added.

As suggested by the Examiner, the title has been amended to recite "Method of testing for atopic dermatitis by measuring expression of the NOR-1 gene." Support for this amendment can be found in the Specification at page 11, lines 18-34.

Claim 1 has been amended to recite a method of testing for "the remission stage of atopic dermatitis that is associated with a decrease in eosinophil cell number in a test subject " using the expression level of the NOR-1 gene as an indicator. The recitation regarding testing for "any allergic disease" has been deleted. Claim 1 has also been amended to recite the correlation step, "wherein the remission stage of atopic dermatitis that is associated with a decrease in eosinophil cell number is indicated by an increase in the level of NOR-1 gene expression in the eosinophil cells of the test subject as compared with that in an atopic dermatitis exacerbation subject" in part (b). Further, Claim 1 has been amended to no longer recite comparison of the NOR-1 gene expression level in the eosinophil cells of a test subject to that in a healthy subject. Claim 1 has been further amended to delete reference to measuring the expression level of the NOR-1 receptor protein as an indicator in the method. Support for the aforementioned amendments to Claim 1 can be found throughout the Specification and, in particular, in Example 1 (at page 36, line 13 - page 44, line 21) and Example 2 (at page 44, line 24 - page 45, line 16).

Claims 54-57 drawn to methods of "assessing the effect of a therapy on the atopic dermatitis" of a test subject or an individual have been added. Support for these new claims can be found in the Specification at page 12, line 30 - page 13, line 10.

The amended claims find support in the application as originally filed. Therefore, this Amendment does not add new matter. Further remarks are set forth below.

Specification

The Examiner states that the current title that reads "...and therapeutic agents for treating same" is not descriptive because it describes a non-elected invention. The title has been amended to recite "Method of testing for atopic dermatitis by measuring expression of the NOR-1 gene" to indicate the invention to which the claims are directed, according to the Examiner's suggestion.

Information Disclosure Statement

The Examiner has acknowledged receipt and consideration of references AA, AB, AL, AN, AP and AR-AT in the Information Disclosure Statements (IDSs) submitted on 6/7/2004 and 11/22/2004. However, the Examiner states that because copies of references AM (EP 1287019), AO (EP 1265628) and AQ (EP 1185647) cited in the IDS submitted on 6/7/2004 have not been provided, that these citations have been crossed out. The Examiner requests that Applicants submit these references in a new IDS.

37 C.F.R. § 1.98(c) states that "[w]hen the disclosures of two or more patents or publications listed in an information disclosure statement are substantially cumulative, a copy of one of the patents or publications as specified in paragraph (a) of this section may be submitted without copies of the other patents or publications, provided that it is stated that these other patents or publications are cumulative. " (MPEP Eighth Ed. Rev. May, 2004, 609, page 600-128, col. 2).

In the IDS submitted on 6/7/2004, Applicants clearly state that reference AM (EP 1287019) corresponds to reference AL (WO 01/87923), reference AO (EP 1265628) corresponds to reference AN (WO 01/70254) and reference AQ (EP 1185647) corresponds to reference AP (WO 00/77202), to indicate that the corresponding references are cumulative. Legible copies of WO 01/87923, WO 01/70254 and WO 00/77202 were provided as required. As EP 1287019, EP 1265628 and EP 1185647 are substantially cumulative with the aforementioned international applications, Applicants were not required to supply copies of the European patent publications.

Furthermore, according to Article 158(1) of the European Patent Convention, international publications published under Article 21 of the Patent Cooperation Treaty in one of the official languages of the European Patent Office (of which English is one) shall take the place of the publication of a European patent application. In the present case, each of the three international publications are written in English and, as such, have taken the place of the corresponding European publications according to Article 158. Applicants request the Examiner consider and indicate consideration of all three European patent publications cited in the IDS submitted on 6/7/2004.

Rejection of Claims 1-3 and 31 Under 35 U.S.C. § 112, First Paragraph

Claims 1-3 and 31 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply

with the enablement requirement, the Examiner stating that the claims contain subject matter that was not described in the Specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner finds the data to be inconclusive as to identifying atopic dermatitis, stating that (1) variations among the individual scores for NOR-1 expression levels in atopic dermatitis patients are large in both the exacerbation stage and the remission stage, (2) no statistical analysis of the results for any of the subjects with atopic dermatitis nor for healthy individuals has been provided, and (3) variations in NOR-1 expression levels for healthy individuals are expected to be great. Further, the Examiner asserts that even if the claims were enabled for a method of testing for the remission stage of atopic dermatitis, that they would not provide enablement for testing for the exacerbation stage of atopic dermatitis, or for any other allergic disease. Finally, the Examiner notes that while the invention may be enabled for measuring specific gene levels, that the claims are not enabled for measuring specific protein levels as it is well known in the art that gene expression is not necessarily an accurate predictor of protein expression.

In Example 1, Applicants teach that expression of the NOR-1 gene is dramatically increased (see Specification, Table 5, at page 43) in association with a significant decrease in the number of eosinophil cells in individuals that have transitioned to the remission stage of atopic dermatitis (see Specification, Table 2, at page 38 and at page 44, lines 1-21), with the decrease in the number of eosinophil cells being a representative clinical marker for improved atopic dermatitis (see Specification, at page 13, lines 6-10). Specifically, Applicants teach that, due to therapy, four out of the seven atopic dermatitis patients (i.e., patient nos. 1, 2, 3 and 5) exhibit a significant decrease in number of eosinophil cells, ranging from a decrease of 858 to 1543 cells, in transition to the remission stage (see Specification, Table 2, at page 38). NOR-1 gene expression levels in the exacerbation stage of patient nos. 1, 2, 3 and 5 range from 53.86 to 454.19 copy/ng RNA with an average of 262.24 copy/ng RNA. Thus, the range of NOR-1 gene expression in patients showing a significant decrease in eosinophil cells with therapy is much smaller than that noted by the Examiner (see Office Action at page 3, line 29 - page 4, line 2). Likewise, Applicants teach that the expression level of the NOR-1 gene in patient nos. 1, 2, 3 and 5 in the remission stage of atopic dermatitis ranges from 167.13 to 5298.42 copy/ng RNA, with an average of 3666.36 copy/ng RNA. Hence, in patients having a dramatic decrease in

eosinophil cell number, there is a clear increase in the average NOR-1 gene expression level in patients in the remission stage of atopic dermatitis (3666.36 copy/ng RNA on average) compared to that in patients in the exacerbation stage of atopic dermatitis (262.24 copy/ng RNA on average), an increase in NOR-1 gene expression confirmed by statistical analysis (see Specification, Table 6, at page 43). Furthermore, NOR-1 gene expression level was not only increased, but prominently elevated in patient nos. 1, 3 and 5 (i.e., 5298.42 copy/ng in patient no. 1, 4546.94 copy/ng in patient no. 3 and 4655.96 in patient no. 5).

Claim 1 has been amended to recite a method of testing for "the remission stage of atopic dermatitis that is associated with a decrease in eosinophil cell number in a test subject " (emphasis added). Recitation of a method of testing for "any allergic disease" has been deleted. Claim 1 has also been amended to recite a comparison step in which the NOR-1 gene expression level in the eosinophil cells of a test subject is compared to that in the eosinophil cells of "an atopic dermatitis exacerbation stage subject." Claim 1 has been further amended to no longer recite a comparison of NOR-1 gene expression in a test subject to that in a healthy subject. Thus, based upon Applicants' teachings, one with skill in the art would be able to test for the remission stage of atopic dermatitis associated with a decrease in eosinophil cell number in an individual by comparing the individual's NOR-1 gene expression level in eosinophil cells to that of subjects having atopic dermatitis in the exacerbation stage.

Claim 1 has also been amended such that the method no longer recites measuring the expression level of the NOR-1 receptor protein and instead only recites measurement of the NOR-1 gene expression level. Claims 3 and 31 have been canceled, obviating the rejection with respect to those claims. Therefore, in view of Applicants' teachings regarding increased NOR-1 gene expression in particular individuals in the remission stage of atopic dermatitis and the amendments to Claim 1, Claim 1 fulfills the enablement requirement of 35 U.S.C. § 112, first paragraph. Claim 2 is dependent on Claim 1 and thus also includes its limitations. Reconsideration and withdrawal of the rejection to Claims 1 and 2 are requested.

New independent Claims 54 and 56 and dependent Claims 55 and 57 recite and include the limitations of Claim 1 and, thus, would also fulfill the enablement requirement of 35 U.S.C. § 112, first paragraph.

Rejection of Claims 1-3 and 31 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3 and 31 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. The Examiner states that Claim 1 is indefinite because it is unclear how comparing the responses leads to the identification required by the preamble (i.e., a method of testing for an allergic disease), and that Claims 2, 3 and 31 are indefinite because they depend from rejected Claim 1 without adding clarity to the method.

Claims 3 and 31 have been canceled, thereby obviating the rejection with respect to those claims. Claim 1 has been amended to recite "wherein the remission stage of atopic dermatitis that is associated with a decrease in eosinophil cell number is indicated by an increase in the level of NOR-1 gene expression in the eosinophil cells of the test subject as compared with that in an atopic dermatitis exacerbation subject" to clarify how the comparison step relates to the method of testing for the remission stage of atopic dermatitis. As such, amended Claim 1 satisfies the requirement of 35 U.S.C. § 112, second paragraph. Claim 2 is directly dependent on Claim 1 and thus includes the limitations of amended Claim 1 such that it also meets the requirement of 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of the rejection are requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,
HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Kamilah Alexander

Kamilah Alexander
Registration No. 57,210
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Dated: 9/13/05